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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,040	07/17/2001	Josef Endl	BMID9814US	8496

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EXAMINER
NGUYEN, BAO THUY L

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/21/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/786,040	Applicant(s) ENDL ET AL.	
	Examiner Bao-Thuy L. Nguyen	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-27* is/are pending in the application.

4a) Of the above claim(s) *16,17 and 22-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Claims 16-17, and 22-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Applicant's election with traverse of Group II, claims 18-21 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the claims of Groups I, II and III are linked so as to form a single general inventive concept and comprise the same or corresponding technical features. Applicant argues that the antibodies of Groups I and II are structurally, chemically, biologically and physiologically related; that the methods of Groups III-V are related because they disclose and recite the detection, isolation or production of antibodies defined by the claims of Groups II and III. This is not found persuasive because the monoclonal antibodies disclosed in Groups I and II are different because they have different binding characteristics. Clearly, the antigen binding portions of the antibodies must be different or else they would be the same antibodies. Therefore, even though the antibodies are recited as binding to the same antigen, they are clearly different antibodies. Furthermore, the methods of groups III, IV and V are clearly different because they are not drawn to methods of detecting, isolating or making the claimed antibodies as argued. The method of Group III is generally a method of detecting antibodies that binds to IA-2 or IA-2ic, these could be autoantibodies to IA-2 or IA-2ic and not the monoclonal antibodies produced in Groups I and II. The method of Group IV is drawn to the isolation of IA-2 antigen and does not relate to the monoclonal antibodies of Groups I and II. And, lastly, the method of group V is drawn to the making of anti-idiotypic antibodies and is not related to the monoclonal antibodies of Groups I and II.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to provide an adequate written description of the invention and fails to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR " 1.801-1.809."

The specification lacks complete deposit information for the claimed monoclonal antibody. Because it is not clear that the claimed antibody is known and publicly available or can be reproducibly isolated without undue experimentation, a suitable deposit for patent purposes is required. Accordingly, filing of evidence of the reproducible production of the antibody is necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above monoclonal antibody, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the

cell lines and isolation of the monoclonal are unpredictable events. Applicants must comply with the criteria set forth in 37 CFR §§ 1.801-1.809.

If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific cell lines have been deposited under the Budapest Treaty, that the cell lines will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the cell lines will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein.

If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR §§ 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
3. the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
4. the deposits were viable at the time of deposit; and,
5. that the deposits will be replaced if they should ever become non-viable.

Applicant's attention is directed to In re Lundak, 773 F.2nd. 1216, 227 USPQ 90 (CAFC 1985) and 37 CRF § 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 112

4. Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a monoclonal antibody that binds to islet cell antigen IA-2 in a manner equivalent to that of an antibody from cell line 96-3-1; however, the specification has not disclosed any characteristics of the antibody being claimed. Although the specification defines the phrase "can bind in an equivalent manner" as antibodies in which there is a detectable epitope overlap with the defined known antibody; however, the specification lacks any description of ~~the~~ an epitope that may overlap claimed antibody. It is well known in the art and as demonstrated by Ackerman et al (Biotechnology and Bioengineering, 1995) that protein microheterogeneities are a common phenomenon that occurs during the production of biologicals, especially complex glycoproteins such as monoclonal antibodies produce by animal cell cultures, therefore, the deposit of one particular monoclonal antibody, does not enable a monoclonal antibody which may have binding properties that are similar, or which may bind the same antigen in an "equivalent" manner because replication of a specific monoclonal antibody is an unpredictable event. Because the claimed monoclonal antibody has not been properly described and because the prior art teaches that microheterogeneities are common in the production of complex glycoprotein such as monoclonal antibodies, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 18-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Endl et al (US 5,888,813)

Endl discloses human monoclonal antibodies of the IgG isotype against human pancreatic islet cells and method for making the same. See columns 2 and 3.

8. Claims 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Solimena et al (the EMBO Journal Vol. 15, No. 9, pp. 2102-2114, 1996).

Since the properties and description of the monoclonal antibody is unclear due to the lack of a deposit or any description in the specification, it can only be determined that the antibody binds to islet cell antigen IA-2, Solimena teaches the monoclonal antibodies that can bind to IA-2 and thus anticipates the claims. See page 2106.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Payton et al (IDS #9) in view of Kohler (Science, 233:1281-1286. 1986).

Payton discloses that ICA 512 or IA-2 has been identified, sequenced and are well known in the art for use in making antibodies. Payton differs from the instant invention in failing to teach monoclonal antibodies to IA-2.

Kohler disclosed a method for producing hybridoma cell lines secreting monoclonal antibodies using lymphocyte fusion techniques. Kohler disclosed that polyclonal antibodies suffers from major disadvantages such as low titers, the polyclonal antibodies are heterogeneous, limited supply and that it is impossible to reproduce the same combination of specific antibodies in a new animal. In contrast, lymphocyte fusion provides the advantages of specificity, unlimited supply of antibody. The use of impure antigens still leads to pure antibody reagents. All specificities can be rescued. Enrichment or specific hybridomas is

possible. A high level of antibody secretion is observed. The hybridoma cell lines can be manipulated to product antibodies not found in nature, and the method is general such that antibodies against any antigen may be produced. See page 1281.

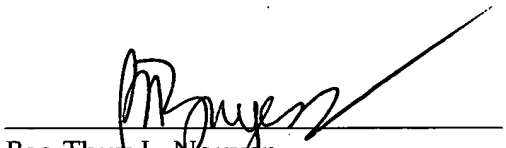
Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a monoclonal antibody against the IA-2 taught by Payton using the method of Kohler because Kohler teaches that any substance that can elicit a humoral response can be used to prepare monoclonal antibodies, and that monoclonal antibodies provides advantages not found in polyclonal antibodies. These advantages include specificity of binding, homogeneity, and ability to be produced in unlimited quantities. The production of monoclonal antibodies allows the isolation of reagents with a unique and chosen specificity. Because all of the antibodies produced by descendants of one hybridoma cell are identical, monoclonal antibodies are powerful reagents for testing for the presence of a desired epitope. In addition, one unique advantage of hybridoma production is that impure antigens can be used to produce specific antibodies. A skilled artisan would have had a reasonable expectation of success and would have been motivated to use the techniques of Kohler to produce monoclonal antibodies to the IA-2 taught by Payton because such techniques are well known in the art and provides advantages not found with polyclonal antibodies.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (703) 308-4243. The examiner can normally be reached on Monday, Wednesday and Thursday from 9:00 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641
July 17, 2003